REMARKS

Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

Claims 1-33 and 42-44 are pending. Claim 1 is amended to clarify particulars of the claim language and to rewrite dependent claims as independent claims. The independent claims are amended so that the preamble is in accord with the result achieved as required by the Examiner. Claim 1 also is amended to recite "individually introducing.." As noted by the Examiner, this limitation, while argued as a basis for novelty of claim 1 was not recited. Amendment of claim 1 should place claim 1 and claims dependent thereon into condition for allowance. The claims that are rewritten as independent claims only are rejected because of the alleged mismatch between the body and the preamble. As noted the preamble as been amended. Accordingly, all claims should be in condition for allowance.

Rejection of Claims Under 35 U.S.C. §112, second paragraph

Claims 1-33 and 42-44 are rejected under 35 U.S.C. §112, second paragraph, because the preamble of claim 1 allegedly is different from the method steps, which identify one or more proteins that have a predetermined property that differs from the target protein." Claim 17 is rejected as indefinite in the recitation of "optimized leads." Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks.

Claims 1-33 and 42-44

The preamble of claim 1 and all claims recite "[a] process for the identification of a protein that differs in a predetermined property from a target protein" As amended the preamble and the result of the method steps are the same. The preamble and the final step of the methods recite "identifying a polypeptide that differs in a predetermined property from a target protein."

Claim 17

Claim 17 is alleged to be indefinite in reciting "optimized lead," because the term is considered vague. The instant specification explains that leads can be further optimized by generating proteins that have combinations of leads. As amended claim 17 no longer refers to the new generated leads as "optimized leads," but recites " new leads that exhibit a greater increase in activity than the leads identified in claim 9," thereby obviating the grounds for the rejection.

Rejection of claim 17 under 35 U.S.C. §112, first paragraph

Claim 17 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement because the recitation "wherein an optimized lead comprises two or more hit positions" allegedly adds new matter. Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks.

While Applicant does not agree that such language adds new matter, amendment of claim 17 to recite that the process results in new leads that have greater activity than the leads of claim 9 renders this ground for rejection moot. Basis for this amendment of claim 17 can be found, for example, in Figure 1 and the legends and description thereof. For example, Figure 1B describes generation of leads. Figure 1C "summarizes the optional next round in which recombination among LEADS is performed to further optimize the LEADS." Claim 17 describes the further steps of recombination and screening to identify leads that are further optimized.

Rejections Under 35 U.S.C. §102

Claims 1-21, 27, and 42-44 are rejected under 35 U.S.C. §102(e) as being anticipated by Short (US Patent No. 6,171,820 B1) because Short discloses a method for producing a set of mutagenized progeny polynucleotides encoding a polypeptide from a parental template polynucleotide via codon site-saturation mutagenesis, wherein at each original codon there is produced at least one substitute codon encoding each of the 20 naturally occurring amino acids. It also is alleged that Short discloses the methods using plasmids and viral vectors in bacterial host cells in addressable arrays, analyzing kinetic activity as improved stability and optionally repeating the steps of the method. This rejection is respectfully traversed.

RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. In re Spada, 15 USPQ2d 1655 (Fed. Cir, 1990), In re Bond, 15 USPQ 1566 (Fed. Cir. 1990), Soundscriber Corp. v. U.S., 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." In re Lang, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover it is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. Lindemann Maschinen-fabrik Gmbh v. American Hoist and

Derrick Co., 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

The Claims

Claim 1 and dependent claims are directed to a process for the identification of a protein that differs in a predetermined property from a target protein. The method includes the steps of (a) producing a population of sets of nucleic acid molecules that encode modified forms of a target protein, (b) **individually** introducing each set of nucleic acid molecules into host cells and expressing the encoded protein, wherein the host cells are present in an addressable array; and(c) individually screening the sets of encoded proteins, whereby one or more proteins that have a predetermined property that differs from the target protein is/are identified. The predetermined property is selected among a chemical, physical and biological property of the target protein. The identified proteins each are designated as a hit and each hit contains a mutation designated a hit position. Dependent claims specify variations of the method including methods of designing and/or synthesizing nucleic acids, methods using addressable arrays, solid supports, types of nucleic acid molecules, variations in the nucleic acids, target proteins and predetermined properties used in the methods and addition steps that can be used with the methods.

The disclosure of Short

Short is directed to mutagenesis techniques for directed evolution of proteins. The patent describes a saturation mutagenesis method that includes generating a set of modified polypeptides in which a full range of amino acid substitutions is represented at each amino acid position. The method uses degenerate oligonucleotide cassettes to generate sets of modified polynucleotides encoding modified polypeptides. In the methods disclosed by Short, each reaction vessel contains at least 32 distinct polynucleotides encoding 20 distinct polypeptides (column 34, lines 43-49). The mixture of polynucleotides is transformed together into host cells and screened.

ANALYSIS

Short does not anticipate the methods as set forth in the instant claims. The methods of the rejected claims include steps of individually introducing and screening sets of nucleic acid molecules each encoding a modified protein in host cells. For example, claim 1 recites that each set of nucleic acid molecules is individually introduced into host cells present in an

addressable array. Thus, the sets of nucleic acids are introduced individually into host cells. Each set of nucleic acids encodes a modified form of a target protein and following introduction into host cells, these modified forms are expressed. The encoded proteins are individually screened in an addressable array and proteins that have a predetermined property that differs from the target protein are identified.

In contrast, the methods disclosed by Short do not include steps of individually introducing and screening sets of nucleic acid molecules each encoding a modified protein. Short specifically states that the saturation mutagenesis described therein involves generating reaction vessels, each of which contains 32 distinct progeny nucleotides. In addition, the 32 distinct progeny nucleotides in each reaction vessel encode 20 distinct polypeptides (column 34, lines 43-60). These mixtures of nucleic acids are amplified in a host (*E. coli*) together. They are not individually introduced into host cells. Therefore Short does not disclose every element as claimed amd does not anticipate any of claims 1-21, 27 and 42-44.

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In view of the above, reconsideration and allowance are respectfully requested

Respectfully submitted,

Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 17109-002001/911
Address all correspondence to:
Stephanie L. Seidman
Fish & Richardson P.C.
12390 El Camino Real
San Diego, California 92130
Telephone: (858) 678-5070
Facsimile: (202) 626-7796
email: seidman@fr.com